

Appl. No. 09/918,421

Amdt. dated July 23, 2003

Reply to Office Action of January 27, 2003

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

6. (currently amended) A method of ~~determining a~~ selecting promising candidate nucleotide sequence sequences of an analytical oligo nucleic acid for use in an analysis of a target nucleic acid, the promising candidate nucleotide nucleotide sequences have a high possibility of including a suitable nucleotide sequence of the analytical oligo nucleic acid, the method comprising:

(a) ~~a first calculation step of entering a nucleotide sequence of a target nucleic acid to be analyzed into a computer;~~

(b) calculating an occurrence frequency of each of n unit sequences occurring on a the nucleotide sequence of a the target nucleic acid to be analyzed on the basis of a value of  $4^n$  which correspond corresponds to all of the n unit sequences formed of n nucleotide sequences, wherein n is an integer of 2 or more;

~~(b) a first extraction step of (c) extracting a sequence all candidate sequences having p number of nucleotides and are present on the nucleotide sequence sequences of a the target~~

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nucleic acid, ~~said~~ wherein  $p$  is an integer larger than  $n$  by  $m$ ,  
wherein ~~and~~  $m$  is an integer of 1 or more;

~~(c) a second calculation step of (d) extracting  $n$  unit  
sequences occurring on the contained in each of the candidate  
sequence sequences; extracted in the first extraction step and  
obtaining an~~

~~(e) calculating an occurrence frequency index of the  
candidate sequence sequences on the nucleotide sequence of the  
target nucleic acid on the basis of the occurrence frequency of  
each of the  $n$  unit sequence calculated in step (b), wherein a  
lower occurrence frequency index indicates a higher specificity  
of the candidate sequences to the target nucleic acid; and~~

~~(d) a second extraction step of (f) selecting, a single or a  
plurality of from the candidate nucleotide sequences extracted in  
step (c), each of the candidate nucleotide sequences each having  
a low lower occurrence frequency index based on than a certain  
threshold value, of the occurrence frequency index obtained from  
the second calculation step, wherein the lower the occurrence  
frequency index, the higher the specificity  
thereby obtaining the promising candidate nucleotide sequences,  
the certain threshold value being arbitrarily set so that the  
promising candidate nucleotide sequences are substantially fewer  
than the candidate nucleotide sequences obtained from step (c)~~

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and the suitable nucleotide sequence being included in the  
promising candidates.

7. (original) The method according to claim 6, wherein said n  
is 5, 6, or 7.

8. (currently amended) The method according to claim 6,  
further comprising ~~a third extraction step of selecting, from the  
promising candidate nucleotide sequences of step (f), a promising  
candidate sequence~~ nucleotide sequences having a low stability of  
a molecular secondary structure which is not capable of forming a  
stable secondary structure, and whereby ~~a sequence~~ more promising  
candidate nucleotide sequences which ~~is~~ are capable of readily  
hybridizing with ~~a~~ the target nucleic acid under hybridization  
conditions ~~is~~ are selected.

9. (previously presented) The method according to claim 8,  
wherein the stability of the molecular secondary structure is  
determined by at least one property selected from the group  
consisting of (i) thermal stability as measured by a value of  $T_m$   
and (ii) stability of an intramolecular secondary structure.

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10. (currently amended) The method according to claim 9, wherein ~~[[,]] in said third extraction step,~~ a nucleotide sequence having the  $T_m$  value falling within a predetermined range is selected from the ~~potential~~ promising candidate nucleotide sequences and forming which forms an unstable secondary structure is further selected.

11. (currently amended) The method according to any one of claims 6 to 10, wherein all of the calculations involved in steps (a) to ~~(d)~~ (f) are sequentially performed by a computer.

12. (previously presented) The method according to any one of claims 6 to 10, wherein said nucleotide sequence of an analytical oligo nucleic acid is used in (i) a PCR method for detecting a specific nucleotide sequence present in a nucleotide sequence of a nucleic acid by using an enzyme reaction which requires hybridization reactions of a nucleic acid, or (ii) in a hybridization reaction of a nucleic acid employing a probe.

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